

What is claimed is:

1. A controlled release oral pharmaceutical composition comprising of:
 - a. therapeutically effective amount of one or more pharmacologically active agents
 - 5 showing low bioavailability;
 - b. one or more solubilizers,
 - c. one or more biocompatible swelling agents, and
 - d. a swelling enhancer.
- 10 2. The controlled release composition of claim 1 wherein the swelling agent in combination with swelling enhancer, swell in the presence of gastric fluid such that the size of the dosage form is sufficiently increased to provide retention of the dosage form in the stomach of a patient, and gradually erode within the gastrointestinal tract over a prolonged time period.
- 15 3. The controlled release oral pharmaceutical composition of claim 1, wherein the pharmacologically active agent is selected from the group consisting of: antiulcer, antidiabetic, anticoagulant, antithrombic, hypolipaeamic, antiarrhythmic, vasodilatory, antianginal, antihypertensive, and vasoprotective agents, fertility enhancers, labour inducers
- 20 and inhibitors, and contraceptive, antibiotic, antifungal, antiviral, anticancer, anti-inflammatory, analgesic, antiepileptic, antiparkinsonian, neuroleptic, hypnotic, anxiolytic, psychostimulatory, antimigraine, antidepressant, antitussive, antihistamine or antiallergic agents.
- 25 4. The controlled release oral pharmaceutical composition of claim 1 wherein the pharmacologically active agent is selected from the group consisting of pentoxifylline, prazosin, acyclovir, levodopa, nifedipine, diltiazem, naproxen, , flurbiprofen, ketoprofen, fenoprofen, fentiazac, oestradiol valerate, metoprolol, sulpiride, captopril, cimetidine, zidovudine, nicardipine, terfenadine, salbutamol, carbamazepine, ranitidine, enalapril,
- 30 simvastatin, fluoxetine, famotidine, ganciclovir, famciclovir, ciprofloxacin, pentazocine, omeprazole, saquinavir, ritonavir, indinavir, nelfinavir, thiamphenicol, calcium carbonate, clarithromycin, azithromycin, ceftazidime, cyclosporine, digoxin, paclitaxel, iron salts, topiramate, and ketoconazole and mixtures thereof.

5. The controlled release oral pharmaceutical composition as of claim 1 wherein the pharmacologically active agent is acyclovir.
6. The controlled release oral pharmaceutical composition of claim 1, wherein the
5 solubilizer is selected from the group consisting of hydrophilic surfactants, lipophilic surfactants and mixtures thereof.
7. The controlled release oral pharmaceutical composition as claimed in claim 1,
10 wherein the solubilizer is selected from anionic, nonionic, cationic, and zwitterionic surfactants.
8. The controlled release oral pharmaceutical composition of claim 1, wherein the solubilizer comprises one or more hydrophilic nonionic surfactants selected from the group consisting of polyethylene glycol sorbitan fatty acid esters and hydrophilic
15 transesterification products of a polyol with at least one member of the group consisting of triglycerides, vegetable oils, and hydrogenated vegetable oils.
9. The controlled release oral pharmaceutical composition of claim 1, wherein the solubilizer is selected from from PEG-20-glyceryl stearate, PEG-40 hydrogenated castor oil,
20 PEG 6 corn oil, lauryl macrogol – 32 glyceride, stearyl macrogol glyceride, polyglyceryl – 10 mono dioleate, propylene glycol oleate, Propylene glycol dioctanoate, Propylene glycol caprylate/caprate, Glyceryl monooleate, Glycerol monolinoleate, Glycerol monostearate, PEG- 20 sorbitan monolaurate, PEG – 4 lauryl ether, Sucrose distearate, Sucrose monopalmitate, polyoxyethylene-polyoxypropylene block copolymer, polyethylene glycol
25 660 hydroxystearate, Sodium lauryl sulphate, Sodium dodecyl sulphate, Proylene glycol alginate, sodium taurocholate, sodium glycocholate, sodium deoxycholate, betains , polyethylene glycol and mixture thereof
10. The controlled release oral pharmaceutical composition of claim 1, wherein the
30 solubilizer is preferably a well-defined mixture of mono-, di-and triglycerides and mono- and di-fatty acid esters of polyethylene glycol.

11. The controlled release oral pharmaceutical composition of claim 1, wherein the ratio of solubilizer to drug preferably is about 20:1 to 1:20.
12. The controlled release oral pharmaceutical composition of claim 1, wherein the ratio
5 of solubilizer to drug preferably is about 10:1 to 1:10.
13. The controlled release oral pharmaceutical composition of claim, wherein the ratio of solubilizer:drug is morepreferably 5:1 to 1:5.
- 10 14. The controlled release oral pharmaceutical of claim 1, wherein the swelling agent is selected from the group consisting of: polyalkylene oxides; cellulosic polymers; acrylic acid and methacrylic acid polymers, and esters thereof, maleic anhydride polymers; polymaleic acid; poly(acrylamides); poly(olefinic alcohol)s; poly(N-vinyl lactams); polyols; polyoxyethylated saccharides; polyoxazolines; polyvinylamines; polyvinylacetates;
15 polyimines; starch and starch-based polymers; polyurethane hydrogels; chitosan; polysaccharide gums; zein; shellac-based polymers; and copolymers and mixtures thereof.
15. The controlled release oral pharmaceutical composition of claim 1, wherein one or more hydrophilic polymer is preferably selected from the group consisting of polyethylene
20 oxide, hydroxypropyl cellulose, hydroxypropyl methyl cellulose, hydroxyethyl cellulose, sodium carboxy methylcellulose, calcium carboxymethyl cellulose, methyl cellulose, polyacrylic acid, maltodextrin, pre-gelatinized starch, polyvinyl alcohol and mixtures thereof.
- 25 16. The controlled release oral pharmaceutical composition of claim 1, wherein one or more hydrophilic polymers is selected from the group consisting of poly(ethylene oxide), poly(ethylene oxide-co-propylene oxide), and mixtures thereof.
17. The controlled release oral pharmaceutical composition of claim 1, wherein the
30 hydrophilic polymer is poly(ethylene oxide).
18. The controlled release oral pharmaceutical composition of claim 1, wherein the content of the hydrophilic polymer in the polymer matrix is about 5 to 90 weight percent.

19. The controlled release oral pharmaceutical composition of claim 1, wherein the weight percent of the hydrophilic polymer in the polymer matrix is preferably about 10 to 70 .

5 20. The controlled release oral pharmaceutical composition of claim 1, wherein the content of the hydrophilic polymer in the polymer matrix is most preferably about 15 to 50 weight percent.

10 21. The controlled release oral pharmaceutical composition of claim 1, wherein the swelling enhancer is selected from the group consisting of low-substituted hydroxypropyl cellulose, microcrystalline cellulose, cross-linked sodium or calcium carboxymethyl cellulose, cellulose fiber, cross-linked polyvinyl pyrrolidone, cross-linked polyacrylic acid, cross-linked Amberlite resin, alginates, colloidal magnesium-aluminum silicate, corn starch granules, rice starch granules, potato starch granules, pregelatinised starch, sodium
15 carboxymethyl starch and mixtures thereof.

22. The controlled release oral pharmaceutical composition of claim 1, wherein the swelling enhancer is selected from the group consisting of cross-linked sodium, calcium carboxymethyl cellulose, cross-linked polyvinyl pyrrolidone, sodium carboxymethyl starch,
20 pregelatinised starch and mixtures thereof.

23. The controlled release oral pharmaceutical composition of claims 1, wherein the swelling enhancer is a cross-linked polyvinyl pyrrolidone.

25 24. The controlled release oral pharmaceutical composition of claims 1, wherein the content of the swelling enhancer is about 5 to 90 weight percent.

25. The controlled release oral pharmaceutical composition of claims 1, wherein the weight percent of the swelling enhancer is about 10 to 70.

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26. The controlled release oral pharmaceutical composition of claim 1, wherein the content of the swelling enhancer is about 15 to 50 weight percent.

27. A pharmaceutical dosage form in the form of an expanding multi-layered system comprising

a first layer property having at least one active pharmaceutical ingredient with an immediate release; and

5 a second layer having at least one active pharmaceutical ingredient with a sustained release property.

28. The pharmaceutical dosage form according to claim 27 wherein the ratio of said active ingredient in said first layer to said active ingredient in said second layer in the range
10 of from about 10:90 to about 90:10 by weight.

29. The solid pharmaceutical composition for oral administration according to claim 27 wherein said first layer further comprises a disintegrating agent selected from group consisting of starch, sodium starch glycolate, pregelatinised starch, crosslinked poly vinyl
15 pyrrolidone, cross linked carboxy methyl cellulose, ion exchange resin and mixtures thereof.

30. The solid pharmaceutical composition for oral administration according to claim 28 wherein said disintegrating agent is present in an amount ranging from about 0.25% to 10%,
20 more preferably about 0.5 to 5.0% and most preferably is about 1% by weight based on the total weight of the composition.

31. A process for preparing a pharmaceutical composition comprising the steps of
solubilizing an active pharmaceutical active ingredient with one or more
25 solubilizers; and

incorporating said solubilized active agent in a gastroretentive matrix having one or more swelling agents and one or more swelling enhancers.

32. The process according to claim 31 wherein the solubilization is done with melt
30 granulation.